Interventions for treating placental abruption (Review)

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[Intervention Review]

Interventions for treating placental abruption

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A B S T R A C T

Background

Placental abruption is an important cause of maternal and fetal mortality and morbidity.

Objectives

To assess the effectiveness and safety of any intervention for the care of women and/or their babies following a diagnosis of placental abruption.

Search methods

The Cochrane Pregnancy and Childbirth Group's Trials Register (16 December 2011).

Selection criteria

Randomised and 'quasi-randomised' trials that report clinically meaningful outcomes and present results on an intention-to-treat basis.

Data collection and analysis

If eligible trials were to be identified, data will be extracted, unblinded, by review authors from all studies.

Main results

No studies that met the inclusion criteria were identified.

Authors' conclusions

The clinical management of placental abruption has to rely on knowledge other than that obtained through randomised clinical trials.

P L A I N   L A N G U A G E   S U M M A R Y

Interventions for treating placental abruption

There is no evidence from trials to show the best way to help pregnant women and babies when there is a placental abruption.

The placenta is attached to the baby by the umbilical cord, and to the inside of the uterus. If the placenta starts separating from the uterus before the baby is born, it is called placental abruption. It can be caused by a medical problem or physical trauma. This quickly becomes life-threatening for women and babies, and cannot be repaired. The baby may need to be delivered immediately, by caesarean section if alive, and often vaginally if the baby has died. Additional treatments include pain relief, blood transfusion and monitoring. However, the review found no trials to show which treatments are best.

BACKGROUND

Placental abruption and placenta praevia are the two major causes of antepartum haemorrhage - vaginal bleeding during the second half of pregnancy. Placenta praevia is a placenta that is situated unusually low in the uterus, and is discussed in a separate Cochrane review (Neilson 2003). Placental abruption is the premature separation of a normally sited placenta, from its attachment to the uterus. Placental abruption is a recognised cause of maternal death (Lewis 1998), especially in resource-poor settings in low-income countries (Prual 2000), and of death of the baby - either because of sudden hypoxia or because of premature delivery. Abruption has been estimated to occur in 6.5 pregnancies per 1000 births, with an associated perinatal mortality rate of 119 per 1000 (compared to 8.2 per 1000 overall in the reference US population) (Ananth 2001a). Placental abruption is twice as common in twin, than singleton, pregnancies (Ananth 2001b).

There are independent associations of placental abruption with other conditions. These include severe fetal growth restriction, prolonged rupture of the membranes, chorioamnionitis (infection of placenta and membranes), hypertension (including pre-eclampsia, non-proteinuric pregnancy-induced hypertension, and pre-existing hypertension), cigarette smoking, advanced maternal age, and unmarried status (Kramer 1997). There is also evidence to link the use of 'crack' cocaine to placental abruption (Miller 1995). Trauma, notably road traffic accidents, may also cause abruption.

Although often considered a 'non-recurring' obstetric complication, the risk of placental abruption was found, in one Swedish study, to rise 10-fold in subsequent pregnancies, to 4% to 5% (Karegard 1986).

Because of the association of placental abruption with hypertensive disease during pregnancy, interventions which might help prevent high blood pressure or the sequelae of hypertension might, in theory, decrease the chances of abruption - this possibility is explored in other Cochrane reviews (e.g. Abalos 2007; Duley 2005; Duley 2007; Hofmeyr 2006).

This review, in contrast, assesses treatments for placental abruption, rather than potential preventative measures. It is worthwhile to consider the clinical features of the condition to identify potential opportunities for useful treatment.

Placental abruption may or may not be associated with obvious vaginal bleeding; that is, the bleeding may be 'revealed' or 'concealed'. Pain over the uterus is a prominent feature. Uterine contractions may start and cause additional, intermittent, pain. Faintness and collapse can occur, as may signs of shock. Typically, the uterus is extremely hard and tender, and it does not relax; fetal parts are difficult to palpate and the fetal heart will be inaudible if death has occurred.

Placental abruption can be a self-extending process with the accumulating blood clot causing more separation, and thus more haemorrhage, until the edge of the placenta is reached. After this, blood can escape through the potential space between the chorion (placental membrane) and the decidua (lining of the uterus during pregnancy) until it reaches the cervix. Blood can also reach the amniotic cavity (by disrupting the placenta, producing blood stained amniotic fluid) and the myometrium (causing the bruised, so-called 'Couvelaire uterus'). There is usually severe fetal hypoxia associated with sizeable placental separation, and sudden fetal death is common.

The major immediate maternal risk is haemorrhagic shock; kidney damage may be seen later in the forms of either acute tubular or cortical necrosis. There may also be clinical and haematological evidence of disordered blood clotting as thromboplastins are released by placental damage and coagulation factors are consumed in the enlarging retroplacental clot at a rate that is faster than the body's ability to replace them.

Placental abruption is essentially a clinical diagnosis, determined by the features described above and confirmed by the demonstration after delivery of a retroplacental clot indenting the placental substance. Ultrasound imaging has a much smaller role than in the diagnosis of placenta praevia. In acute severe abruption, the ultrasound appearances are often unimpressive because the fresh retroplacental clot has acoustic characteristics which may be very similar to those of the placenta itself. In less severe cases in which the pregnancy continues, the clot becomes increasingly echo-free with time, and therefore more obvious to the ultrasonographer (Nyberg 1987).

The traditional, main principles of clinical care of a woman with placental abruption include:

1. early delivery;
2. adequate blood transfusion;
3. adequate analgesia for pain relief;
4. monitoring of maternal condition;
5. assessment of fetal condition.

Early delivery is usual. It has been recommended that, if the baby is alive and the gestation not so early as to make fetal survival extremely unlikely, delivery should be by caesarean section (Rasmussen 1996). Even if the fetus is not obviously hypoxic as a result of placental separation, the effect of the uterine contractions which almost inevitably follow abruption might further compromise the supply of oxygen to the fetus through the placenta. Contractions may also produce shearing forces and therefore the risk of further separation. If the fetus is already dead, as is often the case, it is usual to aim for vaginal delivery.

Prompt treatment and monitoring of the mother is seen as vital. Much of the blood loss from placental abruption is not revealed, and traditional teaching advises that an abruption of sufficient severity to produce fetal death merits a minimum transfusion of two units of blood to the mother.

If there is evidence of coagulopathy (decreased fibrinogen levels, decreased concentrations of platelets, and raised levels of fibrin degradation products), expert haematological input may be required. It has been suggested that high levels of fibrin degradation products might inhibit uterine contractions and make vaginal delivery difficult to achieve in some cases of severe abruption (Basu 1969) as well as contribute to atonic postpartum haemorrhage (excessive blood loss after delivery because of failure of the uterus to contract adequately).

OBJECTIVES

To assess the effectiveness and safety of any intervention for the care of women and/or their babies following a diagnosis of placental abruption.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised and quasi-randomised trials will be included as long as they report clinically meaningful outcomes and present results on an intention-to-treat basis.

Types of participants

Women with a clinical diagnosis of placental abruption, and their babies, whether or not bleeding is revealed.

Types of interventions

Any clinical, or other, intervention specifically designed to improve the care of women or their babies following a diagnosis of placental abruption. Such interventions might include different methods of delivery, or fetal or maternal monitoring, or resuscitation methods or treatments for haematological disturbance.

Types of outcome measures

Indices of maternal outcome (e.g. pain, death, renal failure, uterine rupture, length of stay in intensive care unit, coagulopathy, hysterectomy, impact on future fertility and pregnancies, emotional status), fetal outcome (e.g. death, short- and long-term disability, length of stay in intensive care unit), and obstetric care (e.g. caesarean section, admission to intensive care unit) to include economic data if available.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (16 December 2011).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We did not apply any language restrictions.

Data collection and analysis

Selection of studies

If trials for inclusion are identified in future updates of this review, the following methods will be used.

Two review authors will independently assess for inclusion all the potential studies we identify as a result of the search strategy. We will resolve any disagreement through discussion or, if required, we will consult a third person.

Data extraction and management

We will design a form to extract data. For eligible studies, at least two review authors will extract the data using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third person. Data will be entered into Review Manager software (RevMan 2008) and checked for accuracy.

When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). Any disagreement will be resolved by discussion or by involving a third assessor.

(1) Sequence generation (checking for possible selection bias)

We will describe for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We will assess the method as:

- adequate (any truly random process, e.g. random number table; computer random number generator);
- inadequate (any non random process, e.g. odd or even date of birth; hospital or clinic record number); or
- unclear.

(2) Allocation concealment (checking for possible selection bias)

We will describe for each included study the method used to conceal the allocation sequence in sufficient detail and determine whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We will assess the methods as:

- adequate (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- inadequate (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);

- unclear.

(3) Blinding (checking for possible performance bias)

We will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Studies will be judged at low risk of bias if they were blinded, or if we judge that the lack of blinding could not have affected the results. Blinding will be assessed separately for different outcomes or classes of outcomes.

We will assess the methods as:

- adequate, inadequate or unclear for participants;
- adequate, inadequate or unclear for personnel;
- adequate, inadequate or unclear for outcome assessors.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake. We will assess methods as:

- adequate;
- inadequate;
- unclear.

(5) Selective reporting bias

We will describe for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We will assess the methods as:

- adequate (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- inadequate (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear.

(6) Other sources of bias

We will describe for each included study any important concerns we have about other possible sources of bias.

We will assess whether each study was free of other problems that could put it at risk of bias:

- yes;
- no;
- unclear.

(7) Overall risk of bias

We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008). With reference to (1) to (6) above, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Measures of treatment effect

Dichotomous data

For dichotomous data, we will present results as summary risk ratio with 95% confidence intervals.

Continuous data

For continuous data, we will use the mean difference if outcomes are measured in the same way between trials. We will use the standardised mean difference to combine trials that measure the same outcome, but use different methods.

Unit of analysis issues

Cluster-randomised trials

We will include cluster-randomised trials in the analyses along with individually-randomised trials. Their sample sizes will be adjusted using the methods described in Higgins 2008 using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), or from another source. If ICCs from other sources are used, this will be reported and sensitivity analyses conducted to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomisation unit and perform a separate meta-analysis.

Dealing with missing data

For included studies, levels of attrition will be noted. We will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial will be the number randomised minus any participants whose outcomes are known to be missing.

Assessment of heterogeneity

We will use the I^2 statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity, we will explore it by pre-specified subgroup analysis.

Assessment of reporting biases

Where we suspect reporting bias (see 'Selective reporting bias' above), we will attempt to contact study authors asking them to provide missing outcome data. Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results by a sensitivity analysis.

Data synthesis

We will carry out statistical analysis using the Review Manager software (RevMan 2008). We will use fixed-effect inverse variance meta-analysis for combining data where trials are examining the same intervention, and the trials' populations and methods are judged sufficiently similar. Where we suspect clinical or methodological heterogeneity between studies sufficient to suggest that treatment effects may differ between trials, we will use random-effects meta-analysis.

If substantial heterogeneity is identified in a fixed-effect meta-analysis this will be noted and the analysis repeated using a random-effects method.

R E S U L T S

Description of studies

No studies were identified that met the inclusion criteria.

Risk of bias in included studies

Not relevant.

Effects of interventions

No results were obtained.

D I S C U S S I O N

It is disappointing that no usable clinical trial data are available about such an important clinical problem.

A U T H O R S '   C O N C L U S I O N S

Implications for practice

The clinical management of placental abruption has to rely on knowledge other than that obtained through randomised clinical trials.

Implications for research

All aspects of care of women with placental abruption require further study.

A C K N O W L E D G E M E N T S

None.

REFERENCES

References to studies excluded from this review

Daftary 1983 {published data only}

Daftary SN, Aggarwala V. Antagosan in abruptio-placentae. *Current Therapeutic Research, Clinical and Experimental* 1983;**34**:974-81.

Hall 1972 {published data only}

Hall MH. Folic acid deficiency and abruptio placentae. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1972;**79**:222-5.

Okonofua 1985 {published data only}

Okonofua FE, Olatunbosun OA. Cesarean versus vaginal delivery in abruptio placentae associated with live fetuses. *International Journal of Gynecology & Obstetrics* 1985;**23**:471-4.

References to ongoing studies

El-Sayed 2006 {published data only}

El-Sayed YY. Randomized, double blind trial of magnesium sulfate tocolysis versus intravenous saline for suspected placental abruption (ongoing trial). ClinicalTrials.gov (http://clinicaltrials.gov/) (accessed 21 March 2006).

Additional references

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Basu 1969

Basu HK. Fibrinolysis and abruptio placentae. *Journal of Obstetrics and Gynaecology of the British Commonwealth* 1969;**76**:481-96.

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Duley 2007

Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. *Cochrane Database of Systematic Reviews* 2007, Issue 2. [DOI: 10.1002/14651858.CD004659.pub2]

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Lewis 1998

Lewis G, Drife J, Botting B, Greer I, Kumar C, Neilson J, et al. Why mothers die. Report on confidential enquiries into maternal deaths in the United Kingdom 1994-6. London: HMSO, 1998.

Miller 1995

Miller JM, Boudreaux MC, Regan FA. A case-control study of cocaine use in pregnancy. *American Journal of Obstetrics and Gynecology* 1995;**172**:180-5.

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Neilson JP. Interventions for suspected placenta praevia. *Cochrane Database of Systematic Reviews* 2003, Issue 2. [DOI: 10.1002/14651858.CD001998]

Nyberg 1987

Nyberg DA, Cyr DR, Mack LA, Wilson DA, Shuman WP. Sonographic spectrum of placental abruption. *American Journal of Roentgenology* 1987;**148**:161-4.

Prual 2000

Prual A, Bouvier-Colle MH, de Bernis L, Breart G. Severe maternal morbidity from direct obstetric causes in West Africa: incidence and case fatality rates. *Bulletin of the World Health Organization* 2000;**78**:593-602.

Rasmussen 1996

Rasmussen S, Irgens LM, Bergsjo P, Dalaker K. Perinatal mortality and case fatality after placental abruption in Norway 1967-1991. *Acta Obstetricia et Gynecologica Scandinavica* 1996;**75**:229-34.

RevMan 2008 [Computer program]

The Cochrane Collaboration. Review Manager (RevMan). Version 5.0. Copenhagen, The Nordic Cochrane Centre: The Cochrane Collaboration, 2008.

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Daftary 1983	Trial (based on alternation) tested effects on Antagosan treatment on fibrinogen levels. Sparse details about clinical outcome.
Hall 1972	Trial of folic acid treatment to try to prevent (not treat) placental abruption.
Okonofua 1985	Patient allocation based on alternation but results not presented in intention-to-treat form - 2 women who were allocated to, but declined, caesarean section were reported in the vaginal delivery group. This was a study in Ife-Ife, Nigeria, in which 41 women with clinical diagnoses of placental abruption at > 36 weeks, and with a live fetus, were allocated to vaginal delivery or caesarean section. Electronic fetal heart monitoring was unavailable. 3 of 18 babies (19%) delivered by caesarean section died during the perinatal period, compared to 12 of 23 (52%) after vaginal delivery.

Characteristics of ongoing studies *[ordered by study ID]*

El-Sayed 2006

Trial name or title	Randomised, double blind trial of magnesium sulfate tocolysis versus intravenous saline for suspected placental abruption.
Methods	
Participants	Inclusion criteria: pregnant women, 18 years or older, vaginal bleeding and contractions consistent with suspected placental abruption between 24 and 34 weeks' gestation.
	Exclusion criteria: preterm labour, severe bleeding necessitating immediate delivery, maternal coagulopathy, fetal distress.
Interventions	Magnesium sulfate tocolysis versus intravenous saline.
Outcomes	Primary outcome measures: resolution of vaginal bleeding and contractions.
	Secondary outcome measures: preterm delivery; neonatal outcomes.
Starting date	
Contact information	Yasser Y El-Sayed, MD, Stanford University School of Medicine, Stanford, California, United States, 94305
Notes	NCT00186069

WHAT'S NEW

Date	Event	Description
16 December 2011	New search has been performed	Search updated. No new trials. El-Sayed 2006 still recorded as ongoing.

HISTORY

Protocol first published: Issue 3, 2001
Review first published: Issue 1, 2003

Date	Event	Description
30 April 2009	New search has been performed	Search updated: one ongoing trial added (El-Sayed 2006).
10 August 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

JP Neilson prepared and updated the review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- The University of Liverpool, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Abruptio Placentae [*therapy]

MeSH check words

Female; Humans; Pregnancy